Self-reported Illness and Health Status Among Gulf War Veterans

A Population-Based Study

The Iowa Persian Gulf Study Group

Objective.—To assess the prevalence of self-reported symptoms and illnesses among military personnel deployed during the Persian Gulf War (PGW) and to compare the prevalence of these conditions with the prevalence among military personnel on active duty at the same time, but not deployed to the Persian Gulf (non-PGW).

Design.—Cross-sectional telephone interview survey of PGW and non-PGW military personnel. The study instrument consisted of validated questions, validated questionnaires, and investigator-derived questions designed to assess relevant medical and psychiatric conditions.

Setting.—Population-based sample of military personnel from Iowa.

Study Participants.—A total of 4886 study subjects were randomly selected from 1 of 4 study domains (PGW regular military, PGW National Guard/Reserve, non-PGW regular military, and non-PGW National Guard/Reserve), stratifying for age, sex, race, rank, and branch of military service.

Main Outcome Measures.—Self-reported symptoms and symptoms of medical illnesses and psychiatric conditions.

Results.—Overall, 3695 eligible study subjects (76%) and 91% of the located subjects completed the telephone interview. Compared with non-PGW military personnel, PGW military personnel reported a significantly higher prevalence of symptoms of depression (17.0% vs 10.9%; Cochran-Mantel-Haenszel test statistic, $P<.001$), posttraumatic stress disorder (PTSD) (1.9% vs 0.8%, $P=.007$), chronic fatigue (1.3% vs 0.3%, $P<.001$), cognitive dysfunction (18.7% vs 7.6%, $P<.001$), bronchitis (3.7% vs 2.7%, $P<.001$), asthma (7.2% vs 4.1%, $P=.004$), fibromyalgia (19.2% vs 9.6%, $P<.001$), alcohol abuse (17.4% vs 12.6%, $P=.02$), anxiety (4.0% vs 1.8%, $P<.001$), and sexual discomfort (respondent, 1.5% vs 1.1%, $P=.009$; respondent's female partner, 5.1% vs 2.4%, $P<.001$). Assessment of health-related quality of life demonstrated diminished mental and physical functioning scores for PGW military personnel. In almost all cases, larger differences between PGW and non-PGW military personnel were observed in the National Guard/Reserve comparison. Within the PGW military study population, compared with veterans in the regular military, veterans in the National Guard/Reserve only reported more symptoms of chronic fatigue (2.9% vs 1.0%, $P=.03$) and alcohol abuse (19.4% vs 17.0%, $P=.004$).

Conclusions.—Military personnel who participated in the PGW have a higher self-reported prevalence of medical and psychiatric conditions than contemporary military personnel who were not deployed to the Persian Gulf. These findings establish the need to further investigate the potential etiologic, clinical, pathogenic, and public health implications of the increased prevalence of multiple medical and psychiatric conditions in populations of military personnel deployed to the Persian Gulf.

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A complete list of the members of the Iowa Persian Gulf Study Group appears at the end of this article.

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DURING Operations Desert Shield and Desert Storm, approximately 697 000 US military personnel were deployed to the Persian Gulf theater. These military operations were unique compared with prior service periods in that a large proportion (17%) of deployed personnel were from National Guard and Reserve units, and women were deployed in relatively large numbers (7% of the entire force). Shortly after returning to the United States, some Persian Gulf War (PGW) veterans began to report a variety of symptoms they suspected were related to their military service in the Persian Gulf.[1] The symptoms most commonly reported among PGW veterans were fatigue, joint pain, sleep disorders, memory loss, headache, and rash.[1,2] The population-based frequency of these problems and their causes have not been clearly determined. A variety of possible causes have been postulated for PGW veterans' unexplained illnesses, including infectious agents (eg, leishmaniasis), environmental and ambient pollutants (eg, petroleum and petroleum combustion products, pesticides, chemical agent–resistant coating paint, smoke from oil-well fires, and sand), medical prophylaxis (eg, anthrax and botulinum toxin vaccines and pyridostigmine bromide), depleted uranium munitions, biological and chemical warfare agents, and psychological stressors. However, to date, there has been no convincing epidemiologic or biological evidence that a single illness or cause explains the variety of symptoms PGW veterans are reporting.[1,3-5]

See also pp 215, 223, 231, and 259.

Information regarding the prevalence of illness among PGW veterans has been based on data from self-referred registries established by the Department of Defense and the Department of Veterans Affairs. These Persian Gulf registries have added useful information regarding the spectrum of health concerns among PGW veterans. The most recent analysis of the Department of Defense's Comprehensive Clinical Evaluation Program data on 18 598 Gulf War veterans found no

evidence for a unique illness affecting PGW veterans.[6] Instead, participants reported a wide variety of symptoms affecting multiple organ systems. The most common primary diagnoses were psychological conditions (18.4%), multisystemic conditions (17.9%), and disorders affecting the musculoskeletal system (18.3%). However, these data are of limited value for determining the prevalence and incidence of illnesses because they are not representative of the population of PGW veterans and do not include comparison populations. Obtaining data on a comparable control group of veterans who were not deployed to the Persian Gulf (non-PGW) is essential because the symptoms cited most frequently by PGW veterans are common in the general population.

The purpose of the present study was to assess the prevalence of self-reported symptoms and illnesses among Iowa PGW veterans and to compare these rates with the prevalence of these medical and psychiatric conditions among Iowa non-PGW military personnel. We also explored the relationship between self-reported medical and psychiatric conditions and type of military service (active duty vs National Guard/Reserve). Because of the limited epidemiologic data on the health status of PGW veterans, we used a broad health assessment approach. However, the existing literature[1-6] permitted us to hypothesize that certain medical and psychiatric conditions were more likely to be reported in PGW veterans. The primary medical and psychiatric conditions evaluated were depression, posttraumatic stress disorder (PTSD), chronic fatigue, cognitive dysfunction, and respiratory (airway) disease. Additional medical outcomes also were assessed, including health-related quality of life, fibromyalgia, alcohol abuse, anxiety disorders, injuries, reproductive health, and cancer.

METHODS

Study Population

Two criteria were used to determine which military personnel were eligible for inclusion: (1) Iowa listed as the home of record on the individual's initial military record and (2) service in the regular military or activated National Guard/Reserve some time from August 2, 1990, through July 31, 1991, the PGW period. Listing Iowa as the home of record did not signify that subjects either had recently lived in Iowa or had lived in Iowa for prolonged periods. The Defense Manpower Data Center, Monterey, Calif, operated by the Department of Defense, provided study investigators with identifying demographic and military information for 29 010 military personnel potentially eligible for inclusion in our study. Forty-two of these records were not included in the final study population for various reasons (24 from the pilot study cohort, 14 recalled retirees, 2 incomplete identifiers, and 2 duplicate records). Thus, the final study population consisted of 28 968 persons.

Definitions.—Each individual was classified into 1 of 4 study domains: PGW regular military, PGW National Guard/Reserve, non-PGW regular military, and non-PGW National Guard/Reserve. The PGW cohort was defined as those military personnel who served in the PGW theater some time in the PGW period. The non-PGW cohort was defined as those military personnel who did not serve in the PGW theater but were on active duty or were activated some time within the PGW period. Regular military personnel were defined as those classified as active-duty personnel some time in the PGW period. National Guard/Reserve personnel were defined as those classified as National Guard or Reserve personnel some time in the PGW period. Within each study domain, the population was further stratified by age (≤25 or >25 years), sex, race (white or black/other), rank (officer or enlisted), and branch of service (army, navy/coast guard, air force, or marines). This approach resulted in 64 potential strata within each of the 4 study domains.

Sampling Procedure.—The sample was designed as a stratified random sample with proportional allocation. Subjects who were interviewed in the pilot study were not eligible for the main study sample. Independent samples were selected from each of the 4 domains, with the goal of interviewing 750 subjects from each domain. Subjects were selected for proportional representation in the study domain. However, small strata were oversampled. If a stratum had only 1 subject in the domain, then that subject was selected. If the proportional allocation would have selected fewer than 2 subjects from a stratum, then 2 were selected. The sample was selected in 2 stages. In the first stage, approximately 750 subjects were selected from each domain. After approximately 1600 subjects had been interviewed, we estimated how many additional subjects we would need to add to the sample to attain the goal of 750 subjects interviewed from each domain. Based on these data, a supplementary sample was selected using exactly the same proportions as used for the first stage. This resulted in a final sample size of 4886. The 2 stages of the sample were treated as 1 sample in the analysis. Every effort was made to interview all 4886 subjects.

Medical and Psychiatric Conditions and Exposure Assessment

The specific medical and psychiatric conditions investigated in this study were based on results from published consensus opinions of PGW panels[1-4] and were defined clearly prior to the development of our survey instrument. For both the primary and additional medical and psychiatric conditions, specific symptom patterns were used to define whether an individual's symptoms suggested a particular disorder (or dysfunction). The criteria for these definitions were developed by the study investigators prior to the beginning of the data analysis. Most of the medical and psychiatric conditions were defined based on answers to multiple questions and using accepted criteria from standardized instruments and the medical literature. Self-reported exposures in the Persian Gulf were evaluated based on the number, type, and duration of exposure and the onset of symptoms immediately following exposure. The PGW theater was defined as the Southwest Asia theater of operations (Persian Gulf, Iraq, Kuwait, Saudi Arabia, Red Sea, Gulf of Oman, Gulf of Aden, northern portion of the Arabian Sea, Oman, Bahrain, Qatar, and United Arab Emirates). We divided the PGW subjects into 3 groups based on the area in which the subject reported spending the most time during the PGW period: (1) Iraq, Saudi Arabia, or Kuwait; (2) other countries in the Middle East; or (3) waters bordering the Middle East.

Survey Methods

Instrument Development.—The study instrument was developed by the investigators to assess a broad array of health concerns and to determine the self-reported prevalence of symptoms suggestive of specific medical and psychiatric conditions. Wherever possible, standardized questions, instruments, and scales were used to enhance the validity and generalizability of the results. Sources of questions included the National Health Interview Survey,[7] the Behavioral Risk Factor Surveillance Survey,[8] the Health Status of Vietnam Veterans Telephone Survey,[9] the National Medical Expenditures Survey,[10] the Primary Care Evaluation of Mental Disorders (PRIME-MD),[11] the Brief Symptom Inventory (BSI),[12] the CAGE questionnaire,[13] the PTSD Checklist–Military (PCL-M),[14] the Centers for Disease Control and Prevention Chronic Fatigue Syndrome Questionnaire,[15] the Chalder Fatigue Scale,[16] the American Thoracic Society questionnaire,[17] the Sickness Impact Profile,[18] and questions to assess fibromyalgia,[19] sexual functioning,[20,21] and military exposures.[9,22] The Medical Outcomes Study 36-Item

Short Form (SF-36) was used to assess health-related quality of life.[23] (Additional information regarding case definitions of the medical and psychiatric conditions and for types of PGW exposures is available from the authors on request.)

Recall Bias.—Recall bias was assessed using several approaches. First, the 10-item version of the Marlow-Crowne Social Desirability Scale[24] was included in the questionnaire. This scale measures the tendency to respond to self-report items in a socially desirable fashion and consists of items that describe highly desirable behaviors that have a low probability of occurrence. Second, we determined whether the presence of specific medical and psychiatric conditions interfered with the participant's normal activities. Finally, we determined the relationship between exposures in the Persian Gulf (self-reported and location-dependent) and the presence of medical and psychiatric conditions.

Administration of Survey.—The Statistical Laboratory Survey Section of the Department of Statistics at Iowa State University, Ames, conducted the telephone interviews. The study survey was administered in 2 telephone interviews by trained personnel. An introductory interview was used to obtain the subject's consent and to collect general military and demographic information. The full health and exposure assessments were conducted during the main telephone interview. The introductory interview was administered in approximately 10 minutes (range, 3-30 minutes), and the main interview required approximately 60 minutes (range, 28-185 minutes). The interviews were conducted from September 1995 through May 1996, approximately 5 years after Operation Desert Shield/Desert Storm.

Pilot Study.—The introductory and main interviews were pilot-tested in 24 individuals from the study population and in 3 military personnel outside of the study population. Information from the pilot study was used to refine and finalize the introductory and main interviews. Misunderstood questions were clarified or eliminated.

Locating Strategies.—We used 3 commercial services to identify current addresses and telephone numbers for study subjects: Equifax (McLean, Va), Telematch (Springfield, Va), and Trans Union Corp (Des Moines, Iowa). Letters introducing the study were mailed to subjects with requests to the postal service for forwarding and address correction. The letters also included a toll-free telephone number and postage-paid return card by which the subject could provide new address and telephone information. Additional strategies included the use of Iowa Department of Motor Vehicle records, military base locators, directory assistance services, and national telephone directory CD-ROMs.

Telephone Interviews.—The interview process was initiated by sending an introductory letter and information summary. Within 5 to 7 days of the mailing, a call was made to the subject to explain the study, obtain consent, and conduct the introductory telephone interview. Up to 20 telephone call attempts were made to each respondent in the sample for whom a telephone number could be found, following a standard day, evening, and weekend rotation scheme. If a respondent had not been interviewed after 20 calls, the supervisor evaluated the calling strategy and determined whether additional efforts should be made to contact the potential study subject. If the subject was identified as being institutionalized (including incarcerated), an appropriate institutional administrative authority was consulted to determine the procedures for requesting contact and administering the telephone interview. Telephone interviews were conducted using a computer-assisted telephone interviewing software package (Computer-Assisted Survey Methods Program, University of California, Berkeley).[25]

Survey Administration.—Direct supervision and monitoring continued throughout the data-collection period using a computer-assisted telephone interviewing monitoring program (Lan-Assist, Microtest, Phoenix, Ariz). Ten percent of each interviewer's work was randomly selected and monitored, and the interviewers received regular feedback and evaluation. Supervisory review of all interviews was performed prior to submission for coding and data processing. During the coding phase, when open-ended responses were evaluated and assigned a value, 20% of the coders' work was checked by simultaneous recording and review of the responses. If a coding discrepancy existed, the problem was resolved by supervisory personnel.

Response Reliability.—To assess the test-retest reliability of subjects' responses, approximately 5% of subjects who had completed the introductory and main interviews were systematically sampled in chronological order for re-interview 2 to 4 weeks after completion of the main interview. The subjects in the reliability sample were asked a preselected subset of questions from both the introductory and main interviews.

Data Analysis

The analysis was structured to examine the primary and additional medical and psychiatric conditions in 4 comparisons: all subjects, PGW vs non-PGW; regular military, PGW vs non-PGW; National Guard/Reserve, PGW vs non-PGW; and PGW only, National Guard/Reserve vs regular military. Prevalence was defined as the number of subjects for whom the condition (or outcome) was present, divided by the number of subjects who reported the condition as present, absent, or unknown, presented as a rate per 100 study subjects. Period prevalence rates were calculated, including the 1-year period prior to the telephone interview. Shorter periods were used for specific outcomes, such as injuries (3 months), or for general symptoms (1 month) when available data indicated that a shorter period would be more precise because of potential recall bias. Prior to the study, a 2-tailed α value was established at .05. Ninety-five percent confidence intervals were calculated for each estimate. All statistical analyses were performed using SUDAAN[26] or programmed using SAS[27] to account for the complex sample survey design. Population rates were calculated using SUDAAN. Cochran-Mantel-Haenszel rate differences were calculated using the SAS/IML procedure.[27] Cochran-Mantel-Haenszel rate difference estimates of each of the primary end points were analyzed for the 4 major comparisons, controlling for the stratification variables.[28,29] Rate differences were used rather than rate ratios to emphasize the public health impact of these medical and psychiatric conditions. The relationships between each major medical and psychiatric condition and each category of exposure type were assessed using the Cochran-Mantel-Haenszel χ^2 test, adjusting for the baseline strata. Linear regression was used to compare the mean responses for the health-related quality-of-life scale, with separate regression models fitted for each of the 4 primary comparisons. The regression model included terms for the strata as well as a term for the primary comparisons. The parameter estimate for the term for the primary comparison provided an estimate and SE for the difference between the means for the 2 groups being compared.

The κ coefficients[30] and percentage agreement in responses were calculated for each of the major medical and psychiatric conditions studied.

RESULTS

The sample included 4886 eligible subjects who were proportionately distributed across the strata (age, sex, race, branch of service, and rank) (Table 1). Overall, 3695 (76%) of the eligible study subjects completed a telephone interview. Study subjects in the following strata were less likely to participate in the interview: non-PGW military personnel, regular military personnel, those

Table 1.—Distribution of Eligible Study Subjects and Study Participants Within Relevant Strata*

	Eligible Study Subjects, No.	Telephone Contact, % of Eligible Subjects	Interview Completed	
			% of Eligible Subjects	% of Contacted Subjects
Exposure status				
PGW	2421	84.1	78.3	93.1
Non-PGW	2465	82.6	73.0	88.4
Military status				
Regular military	2627	83.3	74.3	89.3
National Guard/Reserve	2259	83.4	77.1	92.5
Age, y				
≤25	2606	80.8	72.7	90.0
>25	2280	86.3	79.0	91.5
Sex				
Male	4453	83.5	75.5	90.4
Female	433	82.0	77.4	94.4
Race				
White	4624	84.3	76.6	90.9
Black/other	262	66.0	58.0	87.9
Branch				
Army	2767	81.9	75.3	92.0
Air force	668	89.8	79.6	88.7
Marines	649	85.2	77.5	91.0
Navy/coast guard	802	81.6	72.0	88.2
Rank				
Enlisted	4411	82.5	74.8	90.7
Officer	475	91.4	83.6	91.5
Total	**4886**	83.3	75.6	90.7

*PGW indicates Persian Gulf War.

Table 2.—Reported Exposures Among Persian Gulf Military Personnel

	Regular Military (N=985)	National Guard/ Reserve (N=911)
Estimated days in theater, mean (SE)	167.8 (2.5)	138.1 (1.2)
No. of assigned units	820	137
No. of vaccinations (injections and oral), % of subjects		
0	1.5	1.1
1-5	28.3	26.8
6-10	31.1	35.8
>10	33.6	27.1
Missing data	5.5	9.2
No. of pyridostigmine tablets used, % of subjects		
0	45.7	40.8
1-10	17.7	27.0
11-30	14.6	15.0
>30	19.7	12.9
Missing data	2.3	4.3
Smoking history, % of subjects		
Never	44.9	45.1
Former	21.0	22.4
Current	34.1	32.5
Agent, % of subjects		
Solvents/ petrochemicals	88.7	91.2
Smoke/combustion products	85.2	96.0
Sources of infectious agents	84.0	92.6
Psychological stressors	82.6	96.3
Sources of lead from fuels	78.2	88.5
Pesticides	43.8	63.4
Ionizing/nonionizing radiation	27.2	16.0
Chemical warfare agents	4.6	6.4
Physical trauma	3.7	5.6

25 years of age or younger, those with black or other race or ethnic background, navy or coast guard personnel, and enlisted personnel (Table 1). The most important factor associated with participation was our ability to locate the eligible study subject by telephone. Once telephone contact was made with an eligible subject, a high proportion of individuals (87.9%-94.4% across all strata, 90.7% for all study subjects) agreed to participate and completed the interview. A death certificate search of intended participants revealed a total of only 19 deaths in the sample (we estimate that 53 deaths would have been expected).

Among PGW military personnel, differences were observed in the exposures reported by the regular military personnel and the National Guard/Reserve personnel (Table 2). The regular military personnel spent more time in the Persian Gulf than the National Guard/Reserve personnel, who were called to service later during the conflict. The large number of military units represented by the 2 PGW domains (regular military and National Guard/Reserve) suggests a wide range of troop movements and consequent military exposures. Both study groups reported similar total doses of vaccinations, use of pyridostigmine bromide, and exposure to some potentially hazardous agents. The National Guard/Reserve personnel reported higher rates of exposure to smoke/combustion products, pesticides, sources of infectious agents, psychological stressors, and sources of lead from fuels than the regular military personnel.

Compared with non-PGW military personnel, military personnel deployed to the Persian Gulf reported significantly higher prevalence rates of symptoms of depression (major depression, minor depression, chronic dysphoria, and any depression), PTSD, chronic fatigue, cognitive dysfunction, bronchitis, and asthma (Tables 3 and 4). For the major medical and psychiatric conditions, the largest rate difference between PGW and non-PGW military personnel was observed for symptoms of cognitive dysfunction. Among the regular military and National Guard/Reserve personnel, similar differences were observed between PGW and non-PGW military personnel; however, larger differences between PGW and non-PGW military personnel were consistently demonstrated within the National Guard/Reserve comparison (Tables 3 and 4). Among the National Guard/Reserve personnel (but not the regular military personnel), symptoms of bronchitis and asthma were more prevalent among PGW military personnel. Among PGW military personnel, National Guard/Reserve personnel had a higher prevalence of symptoms suggestive of chronic fatigue than regular military personnel. However, no other differences were observed for major medical or psychiatric conditions between the PGW National Guard/Reserve personnel and the PGW regular military personnel. A total of 14.7% of PGW military personnel vs 6.6% of non-PGW military personnel had symptoms of 2 or more medical and psychiatric conditions. Similar differences in the prevalence of 2 or more medical and psychiatric conditions between PGW and non-PGW military personnel were observed for the regular military and National Guard/Reserve study groups.

Although symptoms of fibromyalgia, alcohol abuse, generalized anxiety disorder, and sexual discomfort (respondent and respondent's female partner) were more frequently observed among PGW military personnel, the rate of skin cancer was only marginally elevated in this population, and the rates of aplastic anemia and injury were similar to those observed for non-PGW military personnel (Tables 3 and 4). Similar differences were observed between PGW and non-PGW military personnel within the regular military and National Guard/Reserve study groups. As with major medical and psychiatric conditions, the differences between PGW and non-PGW military personnel were more apparent in the National Guard/Reserve than in the regular military. Among PGW military personnel, National Guard/Reserve personnel were more likely to have symptoms suggestive of alcohol abuse than

Table 3.—Estimated Prevalence of Medical and Psychiatric Conditions*

Condition	PGW Military		Non-PGW Military	
	Regular Military (N=985)	National Guard/ Reserve (N=911)	Regular Military (N=968)	National Guard/ Reserve (N=831)
Depressive symptoms				
Major depression	8.1 (0.8)	10.1 (0.6)	3.9 (0.6)	5.3 (0.6)
Minor depression	15.4 (1.1)	17.5 (0.8)	9.8 (1.0)	11.4 (0.9)
Chronic dysphoria	5.3 (0.7)	8.4 (0.6)	3.2 (0.6)	4.0 (0.5)
Any type of depression	16.4 (1.1)	19.6 (0.8)	10.7 (1.0)	12.6 (0.9)
Symptoms of PTSD†	1.9 (0.4)	2.0 (0.3)	0.7 (0.3)	1.1 (0.3)
Symptoms of chronic fatigue	1.0 (0.3)	2.9 (0.3)	0.2 (0.2)	1.1 (0.3)
Symptoms of cognitive dysfunction	17.7 (1.1)	23.4 (0.9)	7.4 (0.9)	9.5 (0.8)
Symptoms of airway disease				
Bronchitis	3.2 (0.5)	6.2 (0.5)	2.8 (0.6)	1.9 (0.4)
Asthma	6.7 (0.7)	9.4 (0.6)	3.8 (0.6)	6.1 (0.7)
Symptoms of fibromyalgia	18.2 (1.2)	23.8 (0.9)	9.2 (0.9)	13.2 (0.9)
Symptoms of alcohol abuse	17.0 (1.1)	19.4 (0.8)	12.2 (1.1)	16.8 (1.0)
Symptoms of anxiety disorder	3.9 (0.6)	4.5 (0.4)	1.9 (0.4)	1.0 (0.3)
Reported injuries	24.6 (1.3)	24.5 (0.9)	23.0 (1.4)	23.5 (1.2)
Reported impairing injuries	3.6 (0.6)	4.9 (0.4)	3.6 (0.6)	4.5 (0.6)
Any cancer	1.0 (0.3)	1.9 (0.3)	1.0 (0.3)	0.6 (0.2)
Skin cancer	0.8 (0.3)	1.1 (0.2)	0.6 (0.2)	0.2 (0.1)
Aplastic anemia	0.1 (0.1)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Symptoms of sexual discomfort				
Respondent	1.2 (0.3)	2.5 (0.3)	1.1 (0.3)	1.2 (0.3)
Female partner of respondent	5.0 (0.7)	5.4 (0.5)	2.4 (0.5)	2.1 (0.4)

*Values are prevalence rates per 100 study subjects (SE). Rates in each cell depend on the number of subjects responding to each set of items. PGW indicates Persian Gulf War; PTSD, posttraumatic stress disorder.
†Score of 50 or higher on the PTSD Checklist–Military.

Table 4.—Prevalence Differences in Medical and Psychiatric Conditions*

Condition	Prevalence Difference (95% Confidence Interval)†			
	PGW vs Non-PGW			PGW Only, National Guard/ Reserve vs Regular Military
	All Subjects	Regular Military	National Guard/ Reserve	
Depressive symptom				
Major depression	4.0 (2.7 to 5.4)‡	3.6 (1.6 to 5.6)‡	4.5 (2.7 to 6.3)‡	0.2 (−2.2 to 2.6)
Minor depression	5.4 (3.5 to 7.3)‡	4.6 (1.8 to 7.4)‡	6.2 (3.8 to 8.6)‡	−1.2 (−4.2 to 1.8)
Chronic dysphoria	3.0 (1.9 to 4.2)‡	1.8 (0.1 to 3.5)‡	4.4 (2.8 to 6.0)‡	1.3 (−0.7 to 3.2)
Any type of depression	6.0 (4.0 to 7.9)‡	4.7 (1.7 to 7.6)‡	7.4 (4.9 to 9.8)‡	−0.2 (−3.2 to 2.9)
Symptoms of PTSD§	0.9 (0.3 to 1.5)‡	0.9 (−0.1 to 1.9)	0.9 (0.0 to 1.7)‡	−0.9 (−2.1 to 0.3)
Symptoms of chronic fatigue	1.4 (0.9 to 2.0)‡	0.7 (0.1 to 1.3)‡	2.2 (1.3 to 3.1)‡	1.1 (0.1 to 2.2)‡
Symptoms of cognitive dysfunction	10.9 (9.0 to 12.7)‡	8.1 (5.4 to 10.9)‡	13.9 (11.5 to 16.3)‡	2.1 (−1.1 to 5.3)
Symptoms of airway disease				
Bronchitis	2.3 (1.1 to 3.4)‡	0.1 (−1.5 to 1.7)	4.6 (2.8 to 6.3)‡	1.6 (−0.4 to 3.6)
Asthma	2.3 (0.7 to 3.9)‡	1.8 (−0.3 to 3.8)	2.9 (0.5 to 5.2)‡	1.3 (−1.3 to 3.8)
Symptoms of fibromyalgia	9.3 (7.3 to 11.2)‡	7.7 (4.8 to 10.7)‡	11.0 (8.4 to 13.6)‡	0.9 (−2.4 to 4.1)
Symptoms of alcohol abuse	2.4 (0.4 to 4.5)‡	2.3 (−0.8 to 5.4)	2.6 (−0.1 to 5.3)	4.4 (1.4 to 7.4)†
Symptoms of anxiety disorder	2.7 (1.8 to 3.7)‡	1.9 (0.4 to 3.3)‡	3.7 (2.7 to 4.7)‡	−0.4 (−2.0 to 1.3)
Reported injuries	0.5 (−1.9 to 2.9)	−0.2 (3.9 to 3.5)	1.2 (−1.8 to 4.2)	−1.2 (−4.5 to 2.2)
Reported impairing injuries	0.2 (−0.9 to 1.3)	0.3 (−1.3 to 1.9)	0.2 (−1.3 to 1.6)	0.4 (1.2 to 2.0)
Any cancer	0.8 (0.2 to 1.4)‡	0.3 (−0.6 to 1.2)	1.3 (0.6 to 2.0)	0.6 (−0.1 to 1.3)
Skin cancer	0.8 (0.4 to 1.3)‡	0.5 (−0.2 to 1.3)	1.1 (0.6 to 1.6)	0.2 (−0.4 to 0.8)
Aplastic anemia	0.1 (−0.1 to 0.2)	0.1 (−0.1 to 0.4)	0.0 (0.0 to 0.0)	−0.1 (−0.2 to 0.1)
Symptoms of sexual discomfort				
Respondent	0.8 (0.2 to 1.5)‡	0.5 (−0.4 to 1.4)	1.2 (0.3 to 2.1)‡	0.8 (−0.2 to 1.9)
Female partner of respondent	2.8 (1.7 to 4.0)‡	2.2 (0.3 to 4.1)‡	3.6 (2.3 to 4.8)‡	1.0 (−0.8 to 2.8)

*PGW indicates Persian Gulf War; PTSD, posttraumatic stress disorder.
†The Cochran-Mantel-Haenszel rate differences were adjusted for age, sex, race, branch of military, and rank.
‡If the confidence interval does not include 0, ie, no difference in the rates, the prevalence difference is statistically significant ($P \leq .05$).
§Score of 50 or higher on the PTSD Checklist–Military.

regular military personnel. Prevalence rates of self-reported medical conditions not expected to be associated with service in the Persian Gulf, such as aplastic anemia, leukemia, lymphoma, injuries, skin blisters, or skin sores, were not increased in the PGW cohort.

The relationship between self-reported exposures and conditions suggests that no single exposure is related to the medical and psychiatric conditions among PGW military personnel. In fact, among PGW military personnel, most of the self-reported PGW exposures (pyridostigmine use, solvents/petrochemicals, smoke/combustion products, sources of infectious agents, psychological stressors, sources of lead from fuels, pesticides, ionizing/nonionizing radiation, chemical warfare agents, and physical trauma) are significantly related to many of the medical and psychiatric conditions.

For instance, among PGW military personnel, any depression was associated with an increased prevalence of exposure to solvents/petrochemicals (prevalence exposure difference, 6.1; $P<.001$), smoke/combustion products (prevalence exposure difference, 4.5; $P<.001$), sources of infectious agents (prevalence exposure difference, 5.7; $P<.001$), sources of lead from fuels (prevalence exposure difference, 7.4; $P<.001$), pesticides (prevalence exposure difference, 8.7; $P<.001$), ionizing/nonionizing radiation (prevalence exposure difference, 13.4; $P=.03$), chemical warfare agents (prevalence exposure difference, 8.6; $P<.001$), and pyridostigmine use (prevalence exposure difference, 9.4; $P<.001$). Similarly, among PGW military personnel, cognitive dysfunction was associated with an increased prevalence of exposure to solvents/petrochemicals (prevalence exposure difference, 6.6; $P<.001$), smoke/combustion products (prevalence exposure difference 5.1; $P<.001$), sources of lead from fuels (prevalence exposure difference, 8.6; $P<.001$), pesticides (prevalence exposure difference, 14.2; $P<.001$), ionizing/nonionizing radiation (prevalence exposure difference, 15.3; $P<.001$), chemical warfare agents (prevalence exposure difference, 6.8; $P<.001$), pyridostigmine use (prevalence exposure difference, 12.0; $P<.001$), sources of infectious agents (prevalence exposure difference, 5.5; $P<.001$), and physical trauma (prevalence exposure difference, 3.0; $P=.02$). In addition, among PGW military personnel, fibromyalgia was associated with an increased prevalence of exposure to solvents/petrochemicals (prevalence exposure difference, 4.6; $P<.001$), smoke/combustion products (prevalence exposure difference, 5.7; $P<.001$), sources of infectious agents (prevalence exposure difference, 4.8; $P=.001$), psychological

stressors (prevalence exposure difference, 3.4; P=.004), sources of lead from fuels (prevalence exposure difference, 6.7; P<.001), pesticides (prevalence exposure difference, 11.0; P<.001), ionizing/nonionizing radiation (prevalence exposure difference, 12.2; P<.001), chemical warfare agents (prevalence exposure difference, 8.1; P<.001), pyridostigmine use (prevalence exposure difference, 16.4; P<.001), and physical trauma (prevalence exposure difference, 4.9; P<.001).

Place of service within the PGW theater was significantly associated with depression, cognitive dysfunction, and fibromyalgia, with those PGW military personnel who spent most of their time in Iraq, Saudi Arabia, or Kuwait reporting higher prevalence rates of any depression (prevalence exposure difference, 3.1; P=.05), cognitive dysfunction (prevalence exposure difference, 5.2; P<.001), and fibromyalgia (prevalence exposure difference, 6.3; P<.001) than military personnel stationed in other parts of the PGW theater.

Results from the assessment of health-related quality of life as measured by the Medical Outcomes Study SF-36 (Figure) were consistent with the higher prevalence of symptoms of medical and psychiatric conditions among PGW military personnel (Tables 3 and 4). These results demonstrate diminished physical functioning across all subscales, with large absolute differences between PGW and non-PGW military personnel noted for bodily pain, general health, and vitality. Similar differences in health-related quality of life between PGW and non-PGW military personnel were observed within the regular military and National Guard/Reserve study groups (data not shown). However, among PGW military personnel, compared with regular military personnel, National Guard/Reserve personnel were observed to have decreased scores only for general health, vitality, and a composite measure of mental health (data not shown). The SF-36 scores in our study cohort are consistent with those reported in a similar population of young subjects surveyed by telephone.[31] Among PGW military personnel, the self-reported medical and psychiatric conditions were significantly related to self-reports of decreased performance at work and interference with social activities derived from the SF-36.

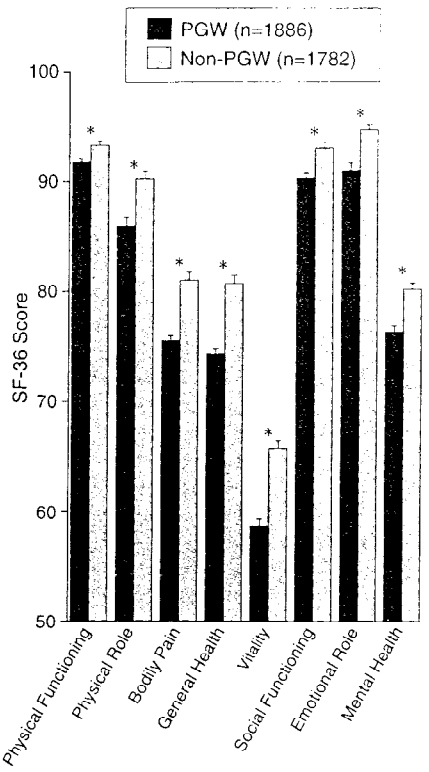
Reliability was tested in approximately 5% of the study population. A total of 184 cases were selected for a reliability interview and 165 reliability interviews were completed. Results indicate a high degree of test-retest agreement (89.6%-97.0%), with κ scores ranging from 0.39 to 0.79 across the medical and psychiatric conditions.

The PGW military personnel had a lower mean±SE Marlow-Crowne Social Desirability score than the non-PGW military personnel (5.36±0.05 vs 5.58±0.06, P=.06), suggesting that PGW military personnel were less likely to be affected by social desirability in responding to questions. In further analyses, we found that statistically significant lower scores for the PGW military personnel applied only to the National Guard/Reserve comparison (P<.001).

COMMENT

Our results indicate that military personnel who participated in the PGW have a higher self-reported prevalence of medical and psychiatric conditions than contemporary military personnel who were not deployed to the Persian Gulf. These medical and psychiatric conditions include symptoms of depression, PTSD, chronic fatigue, cognitive dysfunction, bronchitis, asthma, fibromyalgia, alcohol abuse, anxiety, sexual discomfort, and diminished mental and physical functional health. Although similar qualitative differences in self-reported medical and psychiatric conditions were observed between PGW and non-PGW military personnel among the regular military and the National Guard/Reserve, larger differences in prevalence between PGW and non-PGW military personnel were consistently demonstrated within the National Guard/Reserve comparison. These differences between PGW and non-PGW military personnel establish the need to further investigate the potential clinical implications of these findings. Our findings also highlight the need for additional studies to investigate the etiologic and biological factors that account for these observations.

The finding of a higher prevalence of symptom reporting among PGW veterans has been noted previously.[1,6,32] A cluster investigation of PGW veterans and 3 comparison units found that PGW veterans reported a higher prevalence of 13 chronic symptoms, including depression, memory and concentration difficulties, and fatigue.[32] However, physical examinations and laboratory testing of those reporting symptoms found no pattern of documented abnormalities.[32] Our finding that the PGW veterans self-reported a wide range of medical and psychiatric conditions is similar to the experience of the large case series of the Veterans Affairs Persian Gulf Registry[1] and the Department of Defense Comprehensive Clinical Evaluation Program.[6] In aggregate, these results suggest that PGW veterans report a higher prevalence of medical and psychiatric conditions that involve multiple organ systems. However, it should be noted that some illnesses, such as viscerotopic leishmaniasis, have been found to be unique to PGW veterans.[33]



Results (mean scores, with error bars indicating SE) of the 36-Item Medical Outcomes Study Short Form (SF-36) subscales for all Persian Gulf War (PGW) and non-PGW study subjects. A score of 100 indicates no impairment. Asterisk indicates P<.01.

Several explanations may account for the higher prevalence of self-reported symptoms of medical and psychiatric conditions among PGW veterans. One potential explanation is that a distinct cause or exposure is responsible for each of the self-reported medical and psychiatric conditions. For instance, while inhalation of sulfur dioxide might account for the higher prevalence of bronchitis or asthma, exposure to psychological stressors could contribute to the development of psychiatric conditions (depression, PTSD, and anxiety). An alternative and equally plausible explanation for our findings is that one specific psychiatric condition, such as depression, represents the primary or fundamental medical condition associated with the PGW. This would imply that the other conditions observed more frequently in PGW military personnel represent medical problems that are pathogenically related to depression. Third, exposures or prophylactic measures found to be safe and well-tolerated alone may act synergistically with other exposures encountered in military settings and thus cause more severe disease. Results from a recently published animal study indicate that simultaneous

exposure to large doses of agents used in the Persian Gulf, including insecticides (DEET and permethrin) and pyridostigmine, substantially enhances the overall acute toxic effects of these agents.[34] However, whether these agents act synergistically to cause long-term health effects is less clear. Fourth, the self-reported medical and psychiatric conditions among PGW military personnel potentially involve the central nervous system, lungs, musculoskeletal system, and genitourinary system, raising the possibility that these individuals have a multisystemic condition that does not fit well into an established category of disease. Although this explanation is possible and scientifically intriguing, little evidence exists. Finally, the medical and psychiatric conditions that were reported among PGW military personnel may not be unique to the PGW. These symptoms are analogous to conditions reported by veterans of other wars, dating back to the US Civil War,[35] and may be caused by the experience of warfare rather than by a specific exposure.

An alternative explanation for our finding is differential recall between PGW and non-PGW military personnel. Recall bias, which could substantially alter the frequency of illness or exposures between exposed and nonexposed subjects, is a potential problem in any retrospective epidemiologic study.[36-39] Subjects sensitized by the media or by medical professionals about the possible relationship between adverse exposures and ill health may report more exposures and/or symptoms. However, the extent to which disease and exposure characteristics influence differential recall is not well understood or frequently studied.[37,39] A similar study of Vietnam veterans demonstrated high rates of nonspecific symptoms, although most of their symptoms were not found to be associated with organic disease.[40-44] Similar discrepancies have been reported recently in an investigation of a cluster of unexplained illnesses among PGW veterans in a Pennsylvania Air National Guard unit.[32] Additionally, investigation of reports of frequent birth defects among children of PGW veterans in Mississippi could not confirm an increase in birth defects.[45] A recent investigation demonstrated that mortality rates were higher among veterans deployed to the Persian Gulf than among veterans deployed elsewhere, although most of this increase was caused by unintentional injuries.[46] The PGW military personnel who remained on active duty were not at increased risk of hospitalization in the 2 years after the war.[47] Our study included a wide range of medical and psychiatric illnesses more likely to be evaluated in ambulatory care visits and therefore not addressed by these prior studies. Moreover, results from the Marlow-Crowne Social Desirability Scale and the relationship between the prevalence of medical and psychiatric conditions and both exposures in the PGW theater and diminished functioning at home and at work suggest that these self-reported conditions may represent medical and psychiatric diseases among PGW veterans. However, the results from these analyses should not be overinterpreted, and the degree to which differential recall accounts for our study conclusions can only be assessed by more objective clinical measures of these specific medical and psychiatric conditions.

The PGW National Guard/Reserve personnel reported more symptoms of chronic fatigue, alcohol abuse, and decreased mental health status than the PGW regular military personnel. However, none of the other medical or psychiatric conditions were more prevalent among the PGW National Guard/Reserve personnel than among the PGW regular military personnel. These findings are somewhat anomalous because, compared with the regular military personnel, the National Guard/Reserve personnel spent less time in the PGW theater, were more likely to be involved in combat support roles, and probably had fewer overall environmental exposures. However, the National Guard/Reserve personnel were older, were less prepared for combat, and may have been exposed to different types of psychological stressors.

Several limitations are inherent in the design and execution of this study. First, limiting the study population to subjects with a home of record of Iowa may compromise the generalizability of the results. Iowa has a relatively low proportion of minorities, and some individuals may have unique exposures related to agriculture that could account for some of our findings. However, PGW veterans in this study were distributed throughout the Persian Gulf, as indicated by the large number of military units to which they were assigned during the conflict. This suggests that our study population may have been exposed to a large number of potentially hazardous agents and that these exposures are likely generalizable to other PGW veterans. Second, differential participation by selected demographic subgroups, although relatively minor, may limit our ability to generalize to other populations. However, given the high response rate and participation rate, nonresponse bias is unlikely to explain the observed differences. Third, although the telephone interview included validated instruments that have been tested for most of our medical outcomes, internal validation of the responses was not assessed. Fourth, only limited analyses have been performed to compare rates of self-reported medical and psychiatric conditions among the subjects in different study domains. It is possible that further analyses may provide additional insight into the biological and etiologic relationships of illness in this population. Fifth, the analysis required multiple comparisons that could have revealed statistically significant relationships by chance alone. Because this study was designed to provide an overall description of the self-report status of PGW veterans, we decided not to statistically control for the number of comparisons. Finally, the medical and psychiatric conditions we report are based exclusively on self-reported symptoms and have not been validated by objective physical or laboratory findings.

Results from our study establish the need for further investigation. Additional attention should be given to objective clinical measures to determine whether the self-reported medical and psychiatric conditions represent bona fide clinical illnesses. A second area that needs further investigation is the medical condition of women and minority PGW veterans. Low proportions of women and minority subjects were included in our study population, limiting our ability to address this issue. Future investigations should also focus on the individual and combined effects of potential etiologic factors, such as medications and vaccines, infectious agents, ambient pollutants, depleted uranium, biological and chemical warfare, and psychological stressors. Moreover, the PGW experience, with its attendant social and political ramifications, may have been related to the higher prevalence of self-reported medical and psychiatric conditions within this cohort and should be considered in any investigation that proposes to examine the etiologic basis of these observations. Finally, the clinical and pathologic relevance of these PGW-associated medical and psychiatric conditions, the exposure-response and dose-response basis of these conditions, and the possibility that these multiple conditions represent a novel disease process unique to exposures in the Persian Gulf need to be further characterized.

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